```
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 NEWS  1          Web Page for STN Seminar Schedule - N. America
 NEWS  2  AUG 10  Time limit for inactive STN sessions doubles to 40
                  minutes
 NEWS  3  AUG 18  COMPENDEX indexing changed for the Corporate Source
                  (CS) field
 NEWS  4  AUG 24  ENCOMPLIT/ENCOMPLIT2 reloaded and enhanced
 NEWS  5  AUG 24  CA/CAplus enhanced with legal status information for
                  U.S. patents
 NEWS  6  SEP 09  50 Millionth Unique Chemical Substance Recorded in
                  CAS REGISTRY
 NEWS  7  SEP 11  WPIDS, WPINDEX, and WPIX now include Japanese FTERM
                  thesaurus
 NEWS  8  OCT 21  Derwent World Patents Index Coverage of Indian and
                  Taiwanese Content Expanded
 NEWS  9  OCT 21  Derwent World Patents Index enhanced with human
                  translated claims for Chinese Applications and
                  Utility Models
 NEWS 10  OCT 27  Free display of legal status information in CA/CAplus,
                  USPATFULL, and USPAT2 in the month of November.
 NEWS 11  NOV 23  Addition of SCAN format to selected STN databases
 NEWS 12  NOV 23  Annual Reload of IFI Databases

 NEWS EXPRESS MAY 26 09 CURRENT WINDOWS VERSION IS V8.4,
              AND CURRENT DISCOVER FILE IS DATED 06 APRIL 2009.

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FILE 'HOME' ENTERED AT 13:58:33 ON 30 NOV 2009

=> file registry
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.22       0.22
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FILE 'REGISTRY' ENTERED AT 13:59:00 ON 30 NOV 2009

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 29 NOV 2009 HIGHEST RN 1194232-87-5
DICTIONARY FILE UPDATES: 29 NOV 2009 HIGHEST RN 1194232-87-5

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TSCA INFORMATION NOW CURRENT THROUGH June 26, 2009.

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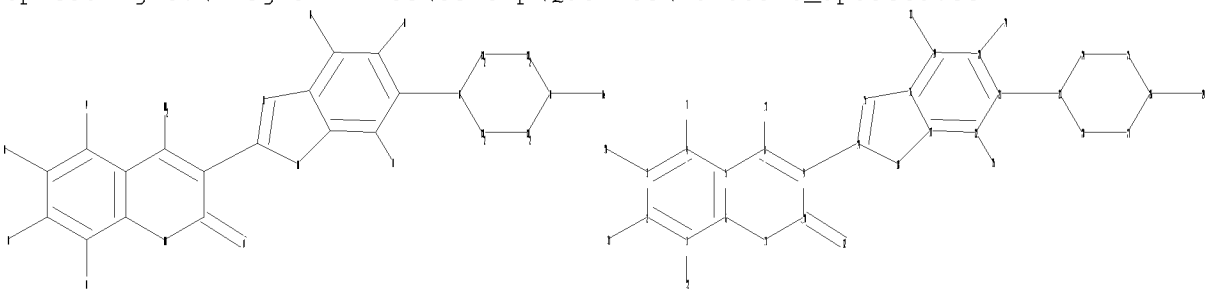
http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Program Files\Stnexp\Queries\10706328_updated.str



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7 12 13 29 30 31 32 33 34 35
ring nodes :
1 2 3 4 5 6 8 9 10 11 14 15 16 17 18 19 20 21 22 23 24 25 26
27 28
chain bonds :
1-32 2-31 3-30 4-7 8-13 9-14 10-12 19-33 20-34 21-23 22-35 26-29
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-8 6-11 8-9 9-10 10-11 14-15 14-18 15-16
16-17 16-19 17-18 17-22 19-20 20-21 21-22 23-24 23-28 24-25 25-26 26-27
27-28
exact/norm bonds :
5-8 6-11 8-9 8-13 9-10 10-11 10-12 14-15 14-18 15-16 17-18 21-23 23-24
23-28 24-25 25-26 26-27 27-28

exact bonds :
1-32 2-31 3-30 4-7 9-14 19-33 20-34 22-35 26-29
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 16-17 16-19 17-22 19-20 20-21 21-22

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:Atom 9:Atom 10:Atom
11:Atom 12:CLASS 13:CLASS 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom
20:Atom 21:Atom 22:Atom 23:Atom 24:Atom 25:Atom 26:Atom 27:Atom 28:Atom
29:CLASS 30:CLASS 31:CLASS 32:CLASS 33:CLASS 34:CLASS 35:CLASS

L1   STRUCTURE UPLOADED

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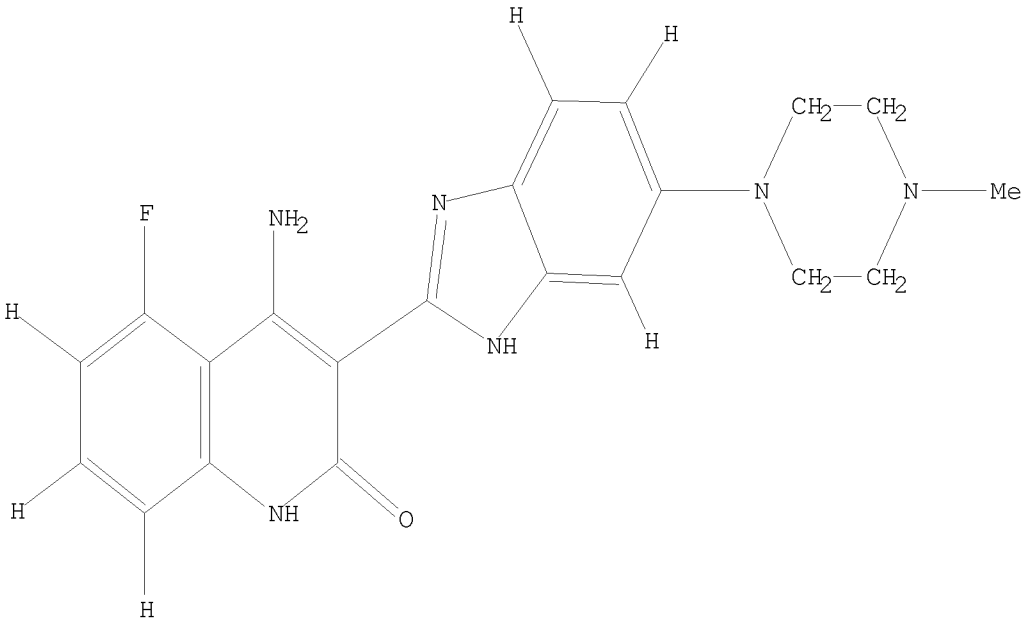
L1 HAS NO ANSWERS
L1   STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1
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SAMPLE SCREEN SEARCH COMPLETED -   75 TO ITERATE

100.0% PROCESSED   75 ITERATIONS   1 ANSWERS
SEARCH TIME: 00.00.03

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS: 981 TO   2019
PROJECTED ANSWERS: 1 TO   80

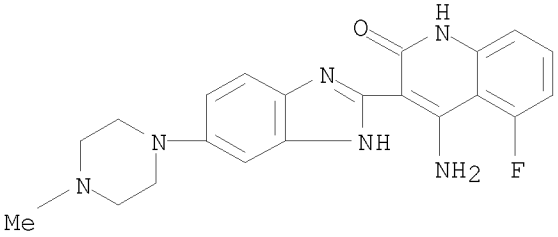
L2   1 SEA SSS SAM L1

=> d l2

L2 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2009 ACS on STN
RN 915769-50-5 REGISTRY
ED Entered STN: 18 Dec 2006
CN Propanoic acid, 2-hydroxy-, compd. with
    4-amino-5-fluoro-3-[6-(4-methyl-1-piperazinyl)-1H-benzimidazol-2-yl]-2(1H)-
    quinolinone, hydrate (1:1:1) (CA INDEX NAME)
MF C21 H21 F N6 O . C3 H6 O3 . H2 O
SR CA
LC STN Files: CA, CAPLUS, CHEMCATS, IMSRESEARCH, PHAR, PROUSDDR, SYNTHLINE,
      TOXCENTER, USAN

    CM 1

    CRN 405169-16-6
    CMF C21 H21 F N6 O



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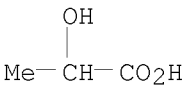

              2 REFERENCES IN FILE CA (1907 TO DATE)
              2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 185.40 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 13:59:55 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -   1493 TO ITERATE

100.0% PROCESSED   1493 ITERATIONS   34 ANSWERS
SEARCH TIME: 00.00.01

L3   34 SEA SSS FUL L1

=> s l1 sss
SAMPLE SEARCH INITIATED 14:00:02 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -   75 TO ITERATE

100.0% PROCESSED   75 ITERATIONS   1 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 981 TO 2019
PROJECTED ANSWERS: 1 TO 80

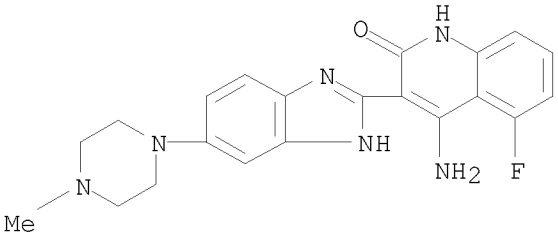
L4 1 SEA SSS SAM L1

=> d l4

L4 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2009 ACS on STN
RN 915769-50-5 REGISTRY
ED Entered STN: 18 Dec 2006
CN Propanoic acid, 2-hydroxy-, compd. with
4-amino-5-fluoro-3-[6-(4-methyl-1-piperazinyl)-1H-benzimidazol-2-yl]-2(1H)-quinolinone, hydrate (1:1:1) (CA INDEX NAME)
MF C21 H21 F N6 O . C3 H6 O3 . H2 O
SR CA
LC STN Files: CA, CAPLUS, CHEMCATS, IMSRESEARCH, PHAR, PROUSDDR, SYNTHLINE, TOXCENTER, USAN

CM 1

CRN 405169-16-6
CMF C21 H21 F N6 O



CM 2

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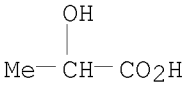

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file caplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 190.46 190.68

FILE 'CAPLUS' ENTERED AT 14:00:29 ON 30 NOV 2009
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FILE COVERS 1907 - 30 Nov 2009 VOL 151 ISS 23
FILE LAST UPDATED: 29 Nov 2009 (20091129/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2009

CAplus now includes complete International Patent Classification (IPC)
reclassification data for the third quarter of 2009.

This file contains CAS Registry Numbers for easy and accurate
substance identification.

During November, try the new LSUS format of legal status information
in the CA/CAplus family databases for free! Complete details on the
number of free displays and other databases participating in this
offer appear in NEWS 10.

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L5          70 L3

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        758861 ?TUMOR?
          6753 ?TUMOUR?
          6753 ?TUMOUR?
        759258 ?TUMOR?
                 (?TUMOR? OR ?TUMOUR?)
          6753 ?TUMOUR?
        758861 ?TUMOR?
        758861 ?TUMOR?
        759258 ?TUMOUR?
                 (?TUMOUR? OR ?TUMOR?)
        588351 ?NEOPLASM?
L6          54 L5 AND (?CANCER? OR ?TUMOR? OR ?TUMOUR? OR ?NEOPLASM?)

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       4773453 AD<20031107
                 (AD<20031107)
L7           5 L6 AND AD<20031107

=> d l7 1-5 ibib abs

L7   ANSWER 1 OF 5  CAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:        2005:1242789  CAPLUS
DOCUMENT NUMBER:         143:477969
TITLE:                   Preparation of benzimidazole quinolinones for
                         inhibiting FGFR3 and treating multiple myeloma
```

INVENTOR(S): Cai, Shaopei; Chou, Joyce; Harwood, Eric; Heise, Carla C.; Machajewski, Timothy D.; Ryckman, David; Shang, Xiao; Wiesmann, Marion; Zhu, Shuguang
PATENT ASSIGNEE(S): Chiron Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 239 pp., Cont.-in-part of U.S. Ser. No. 644,055.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
US 20050261307	A1	20051124	US 2004-983174		20041105	
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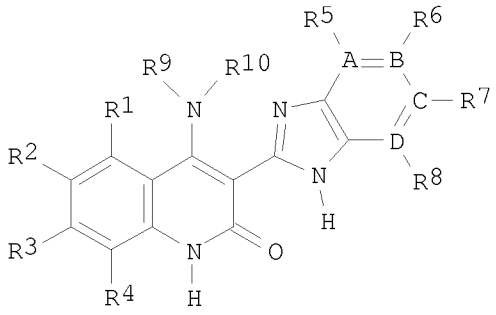
US 7470709	B2	20081230				
CN 1692112	A	20051102	CN 2003-824565		20030819	<--
US 20050203101	A1	20050915	US 2004-839793		20040505	
ZA 2006003598	A	20080430	ZA 2006-3598		20060505	
US 20090281100	A1	20091112	US 2008-317493		20081223	
US 20090181979	A1	20090716	US 2009-398130		20090304	

PRIORITY APPLN. INFO.:

US 2002-405729P	P	20020823
US 2002-426107P	P	20021113
US 2002-426226P	P	20021113
US 2002-426282P	P	20021113
US 2002-428210P	P	20021121
US 2003-460327P	P	20030403
US 2003-460328P	P	20030403
US 2003-460493P	P	20030403
US 2003-478916P	P	20030616
US 2003-484048P	P	20030701
US 2003-644055	A2	20030819
US 2003-517915P	P	20031107
US 2003-526425P	P	20031202
US 2003-526426P	P	20031202
US 2004-546017P	P	20040219
US 2004-982543	B1	20041105

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 143:477969
GI



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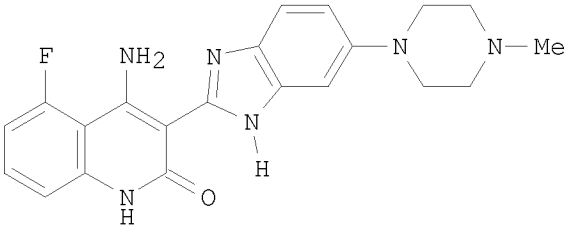

II

AB The title compds. I [A, B, C, and D = C, N; R1-R3 = H, halo, CN, NO2, etc.; R4 = H, alkyl; R5-R8 = H, halo, CN, NO2, etc.; R9 = H, (un)substituted alkyl, aryl, etc.; R10 = H], useful for inhibiting fibroblast growth factor receptor 3 or treating a biol. condition mediated by fibroblast growth factor receptor 3, were prepared E.g., a multi-step synthesis of 4-amino-5-fluoro-3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-quinolin-2-one (II), starting from 5-chloro-2-nitroaniline and 1-methylpiperazine, was given. The majority of the exemplary compds. I displayed an IC50 of less than 10 μM with respect to VEGFR1, VEGFR2, VEGFR3, FGFR1, CHK1, Cdc2, GSK-3, NEK-2, Cdk2, Cdk4, MEK1, NEK-2, CHK2, CK1ε, Raf, Fyn, Lck, Rsk2, PAR-1, c-Kit, c-ABL, p60src, FGFR3, FLT-3, PDGFRα, and PDGFRβ. In addition, many of the exemplary compds. exhibited IC50 values in the nM range and show potent activity with respect to VEGFR1, VEGFR2, VEGFR3, FGFR1, FGFR3, c-Kit, c-ABL, FLT-3, CHK1, Cdc2, GSK-3, NEK-2, Cdk2, MEK1, CHK2, Fyn, Lck, Rsk2, PAR-1, PDGFRα, and PDGFRβ with IC50 values of less than 1 μM. The mentioned above compound II was tested in various tests and showed significant antiproliferative activity. II inhibited FGFR3 receptor phosphorylation and ERK phosphorylation in multiple myeloma cell lines with activating FGFR3 mutations.

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

L7 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:1223876 CAPLUS

DOCUMENT NUMBER: 143:477966

TITLE: Preparation of benzimidazole quinolinones for inhibiting a checkpoint kinase 1 and their use in combination therapy for cancer

INVENTOR(S): Gesner, Thomas G.; Barsanti, Paul A.; Harrison, Stephen D.; Ni, Zhi-Jie; Brammeier, Nathan M.; Zhou, Yasheen; Le, Vincent P.

PATENT ASSIGNEE(S): Chiron Corporation, USA

SOURCE: U.S. Pat. Appl. Publ., 249 pp., Cont.-in-part of U.S. Ser. No. 644,055.
CODEN: USXXCO

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
US 20050256157	A1	20051117	US 2005-41191		20050121	
US 20040092535	A1	20040513	US 2003-644055		20030819	<--
US 7470709	B2	20081230				
CN 1692112	A	20051102	CN 2003-824565		20030819	<--
US 20050203101	A1	20050915	US 2004-839793		20040505	
US 20090281100	A1	20091112	US 2008-317493		20081223	
PRIORITY APPLN. INFO.:			US 2002-405729P	P	20020823	
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			US 2003-460493P	P	20030403	
			US 2003-478916P	P	20030616	
			US 2003-484048P	P	20030701	
			US 2003-644055	A2	20030819	
			US 2004-538984P	P	20040123	

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 143:477966; MARPAT 143:477966
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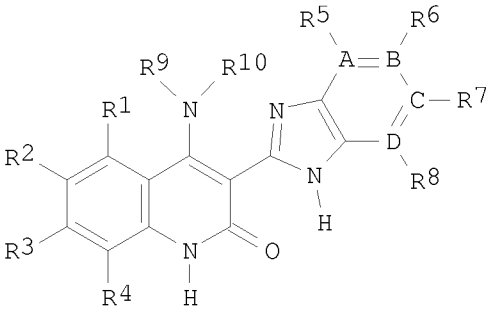

I

AB The title compds. [I; A, B, C, D = C, N; R1 = H, halo, CN, NO2, etc.; R2, R3 = H, halo, NO2, CN, etc.; R4 = H, (un)substituted alkyl; R5, R8 = H, (un)substituted alkyl, alkenyl, heterocyclyl; or R5 may be absent if A = N; or R8 may be absent if D = N; R6, R7 = H, halo, NO2, CN, etc.; R9 = H, (un)substituted alkyl, aryl, etc.; R10 = H; or R9 and R10 join together to form one or more rings, each having 5-7 members], useful for inhibiting checkpoint kinase 1, inducing cell cycle progression, and increasing apoptosis in cells, were prepared E.g., a multi-step synthesis of 4-amino-3-(benzimidazol-2-yl)-6-(4-methylpiperazinyl)hydroquinolin-2-one, was given. The compds. I were tested against various kinases. Two of the prepared compds. I, 4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-chloroquinolin-2-(1H)-one and 6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-4-[(piperidin-2-ylmethyl)amino]quinolin-2(1H)-one, were found to be potent inhibitors of CHK1 with IC50 of 0.32 nM and 0.63 nM, resp. The majority of the exemplary compds. I displayed an IC50 of less than 10 μM with respect to VEGFR1, VEGFR2, VEGFR3, FGFR1, CHK1, Cdc2, GSK-3, NEK-2, Cdk2, Cdk4, MEK1, NEK-2, CHK2, CK1ε, Raf, Fyn, Lck, Rsk2, PAR-1, c-Kit, c-ABL,

p60src, FGFR3, FLT-3, PDGFRα, and PDGFRβ. In addition, many of the exemplary compds. exhibited IC50 values in the nM range and show potent activity with respect to VEGFR1, VEGFR2, VEGFR3, FGFR1, FGFR3, c-Kit, c-ABL, FLT-3, CHK1, Cdc2, GSK-3, NEK-2, Cdk2, MEK1, CHK2, Fyn, Lck, Rsk2, PAR-1, PDGFRα, and PDGFRβ with IC50 values of less than 1 μM. The compds. I may be used to prepare pharmaceutical compns. and may be used in conjunction with DNA damaging agents.

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

L7 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:182836 CAPLUS
DOCUMENT NUMBER: 140:235711
TITLE: Preparation of benzimidazole quinolinones for inhibiting a serine/threonine kinase
INVENTOR(S): Barsanti, Paul A.; Bussiere, Dirksen; Harrison, Stephen D.; Heise, Carla C.; Jansen, Johanna M.; Jazan, Elisa; Machajewski, Timothy D.; Mcbride, Christopher; McCrea, William R.; Ng, Simon; Ni, Zhi-Jie; Pecchi, Sabina; Pfister, Keith; Ramurthy, Savithri; Renhowe, Paul A.; Shafer, Cynthia M.; Silver, Joel B.; Wagman, Allan; Weismann, Marion
PATENT ASSIGNEE(S): Chiron Corporation, USA
SOURCE: PCT Int. Appl., 570 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
WO 2004018419	A2	20040304	WO 2003-US25990		20030819	<--
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG						
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IN 2005KN00484	A	20060106	IN 2005-KN484		20050323	
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			US 2002-426107P	P	20021113	
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OTHER SOURCE(S): MARPAT 140:235711

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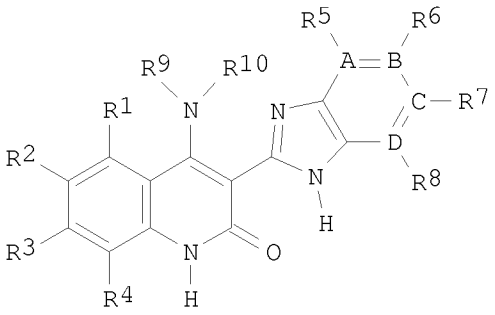

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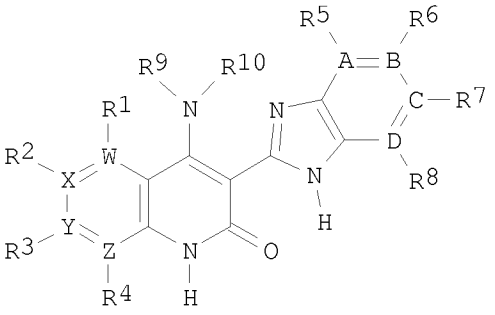

II

AB The title compds. [I and II; A, B, C, and D = C, N; W, X, Y and Z = C, N and at least one of W, X, Y, and Z = N; R1-R8 = H, halo, CN, NO2, etc.; R9 = H, (un)substituted alkyl, aryl, etc.; R10 = H; or NR9R10 = 5-7 membered ring], useful for inhibiting various enzymes and treating various conditions, were prepared E.g., a multi-step synthesis of 4-amino-3-(benzimidazol-2-yl)-6-(4-methylpiperazinyl)hydroquinolin-2-one, was given. The majority of the exemplary compds. I displayed an IC50 of less than 10 μM with respect to VEGFR1, VEGFR2, VEGFR3, FGFR1, CHK1, Cdc2, GSK-3, NEK-2, Cdk2, Cdk4, MEK1, NEK-2, CHK2, CK1ε, Raf, Fyn, Lck, Rsk2, PAR-1, c-Kit, c-ABL, p60src, FGFR3, FLT-3, PDGFRα, and PDGFRβ. In addition, many of the exemplary compds. exhibited IC50 values in the nM range and show potent activity with respect to VEGFR1, VEGFR2, VEGFR3, FGFR1, FGFR3, c-Kit, c-ABL, FLT-3, CHK1, Cdc2, GSK-3, NEK-2, Cdk2, MEK1, CHK2, Fyn, Lck, Rsk2, PAR-1, PDGFRα, and PDGFRβ with IC50 values of less than 1 μM.

OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)

L7 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2003:98039 CAPLUS

DOCUMENT NUMBER: 138:153534

TITLE: Preparation of benzimidazolyl-substituted quinolinone derivatives and analogs, with inhibitory action against vascular endothelial growth factor receptor tyrosine kinase, and useful as anticancer agents

INVENTOR(S): Renhowe, Paul A.; Pecchi, Sabina; Machajewski, Timothy D.; Shafer, Cynthia M.; Taylor, Clarke; McCrea,

	William R.; McBride, Christopher; Jazan, Elisa
PATENT ASSIGNEE(S):	Chiron Corporation, USA
SOURCE:	U.S. Pat. Appl. Publ., 69 pp., Cont.-in-part of U.S. Pat. Appl. 2002 107,392.
	CODEN: USXXCO
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20030028018	A1	20030206	US 2002-116117	20020405 <--
US 20020107392	A1	20020808	US 2001-951265	20010911 <--
US 6605617	B2	20030812		
EP 1650203	A1	20060426	EP 2005-17665	20010911 <--
EP 1650203	B1	20080220		
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EP 1849782	A1	20071031	EP 2007-11978	20010911 <--
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US 20030158224	A1	20030821	US 2002-284017	20021030 <--
US 6774237	B2	20040810		
US 20040006101	A1	20040108	US 2003-387355	20030312 <--
US 6762194	B2	20040713		
CA 2481055	A1	20031023	CA 2003-2481055	20030404 <--
WO 2003087095	A1	20031023	WO 2003-US10463	20030404 <--
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003226275	A1	20031027	AU 2003-226275	20030404 <--
AU 2003226275	B2	20090723		
EP 1497287	A1	20050119	EP 2003-746614	20030404 <--
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BR 2003008996	A	20050222	BR 2003-8996	20030404 <--
CN 1659165	A	20050824	CN 2003-812909	20030404 <--
JP 2005527587	T	20050915	JP 2003-584051	20030404 <--
NZ 536068	A	20080430	NZ 2003-536068	20030404 <--
SG 143985	A1	20080729	SG 2006-6999	20030404 <--
US 20040097545	A1	20040520	US 2003-613411	20030703 <--
US 6800760	B2	20041005		
US 20050054672	A1	20050310	US 2004-886950	20040708
US 7598268	B2	20091006		
MX 2004009739	A	20050111	MX 2004-9739	20041005
IN 2004KN01494	A	20070601	IN 2004-KN1494	20041006
NO 2004004776	A	20041207	NO 2004-4776	20041103
US 20050209456	A1	20050922	US 2005-92137	20050329
US 7335774	B2	20080226		
JP 2007191486	A	20070802	JP 2007-62683	20070312
US 20080070906	A1	20080320	US 2007-866296	20071002
IN 2008KN03126	A	20090206	IN 2008-KN3126	20080730
PRIORITY APPLN. INFO.:			US 2000-232159P P	20000911
			US 2001-951265 A2	20010911

EP 2001-973722	A3	20010911
EP 2005-17665	A3	20010911
JP 2002-526851	A3	20010911
US 2002-116117	A	20020405
US 2002-284017	A1	20021030
WO 2003-US10463	W	20030404
US 2004-886950	A1	20040708
IN 2004-KN1494	A3	20041006

OTHER SOURCE(S): MARPAT 138:153534
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. of formulas I and II are provided [for I: Z = O, S, (un)substituted NH; Y = certain OH derivs., CHO, esters and amides of CO2H, certain NH2 derivs.; R1-R4 = H, halo, cyano, NO2, OH or derivs., NH2 or derivs., (un)substituted amidinyl, guanidinyl, alk(en/yn)yl, aryl, heterocyclyl, CHO, CO2H and esters and amides; R5-R8 = H, halo, NO2, OH or derivs., NH2 or derivs., SH or derivs., cyano, etc.; R9 = H, OH, (un)substituted alkoxy or aryloxy, NH2 or derivs., (un)substituted alkyl or aryl, CHO, alkanoyl, aroyl; for II: A, B, D, E = C or N, with at least one being N; Y = H, OH or derivs., SH or derivs., NH2 or derivs., cyano, various acyl groups, (un)substituted alk(en/yn)yl, aralkyl, heterocycloalkyl, aryl, etc.; R1-R8 = H, halo, NO2, cyano, OH or derivs., NH2 or derivs., acyl, SH or derivs., etc.; R9 = H, OH, (un)substituted alkoxy, aryloxy, NH2 or derivs., aryl, CHO, alkanoyl, aroyl]. Also provided are pharmaceutical formulations including the compds. or their pharmaceutically acceptable salts and a pharmaceutically acceptable carrier, which may be prepared by mixing the compds. or salts with a carrier and water. A disclosed method of treating a patient includes administering a pharmaceutical formulation according to the invention to a patient. Claims include tautomers of the compds., pharmaceutically acceptable salts, and pharmaceutically acceptable salts of the tautomers. I and II are inhibitors of receptor tyrosine kinases, and particularly of vascular endothelial growth factor receptor (VEGFR) tyrosine kinase. As such, they are inhibitors of angiogenesis, and thereby act as anticancer agents. Approx 270 invention compds. are listed, with detailed prepns. given for about 50 compds. Several general preparatory methods are discussed in detail. For instance, cyclocondensation of Et 2-(benzimidazol-2-yl)acetate with the corresponding ortho-amino nitrile (prepns. given), carried out in refluxing ClCH2CH2Cl in the presence of SnCl4, gave the invention quinolinone III. Many compds. I and II had in vitro IC50 values of less than 10 μM with respect to flt-1 (VEGFR1), KDR (VEGFR2) and bFGF kinases (recombinant, expressed in Sf9 insect cells).

OS.CITING REF COUNT: 12 THERE ARE 12 CAPLUS RECORDS THAT CITE THIS RECORD (12 CITINGS)

L7 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2002:220574 CAPLUS
DOCUMENT NUMBER: 136:263158
TITLE: Benzimidazolyl-substituted quinolinone derivatives and analogs, with inhibitory action against vascular endothelial growth factor receptor tyrosine kinase, and useful as anticancer agents
INVENTOR(S): Renhowe, Paul; Pecchi, Sabina; Machajewski, Tim; Shafer, Cynthia; Taylor, Clarke; McCrea, Bill; McBride, Chris; Jazan, Elisa; Wernette-Hammond, Mary-Ellen; Harris, Alex

PATENT ASSIGNEE(S): Chiron Corporation, USA
SOURCE: PCT Int. Appl., 207 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002022598	A1	20020321	WO 2001-US42131	20010911 <--
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CA 2421120	A1	20020321	CA 2001-2421120	20010911 <--
CA 2421120	C	20080715		
AU 2001093275	A	20020326	AU 2001-93275	20010911 <--
EP 1317442	A1	20030611	EP 2001-973722	20010911 <--
EP 1317442	B1	20051116		
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HU 2003001045	A2	20031229	HU 2003-1045	20010911 <--
BR 2001013757	A	20040302	BR 2001-13757	20010911 <--
JP 2004509112	T	20040325	JP 2002-526851	20010911 <--
JP 4361727	B2	20091111		
NZ 524717	A	20040924	NZ 2001-524717	20010911 <--
AU 2001293275	B2	20050414	AU 2001-293275	20010911 <--
AT 309996	T	20051215	AT 2001-973722	20010911 <--
ES 2250480	T3	20060416	ES 2001-973722	20010911 <--
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EP 1650203	B1	20080220		
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EP 1849782	A1	20071031	EP 2007-11978	20010911 <--
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CN 100351249	C	20071128	CN 2001-815371	20010911 <--
AT 386736	T	20080315	AT 2005-17665	20010911 <--
ES 2302106	T3	20080701	ES 2005-17665	20010911 <--
ZA 2003001578	A	20040826	ZA 2003-1578	20030226 <--
IN 2003KN00244	A	20050311	IN 2003-KN244	20030226 <--
MX 2003002032	A	20030724	MX 2003-2032	20030307 <--
NO 2003001097	A	20030325	NO 2003-1097	20030310 <--
NO 324155	B1	20070903		
US 20040006101	A1	20040108	US 2003-387355	20030312 <--
US 6762194	B2	20040713		
BG 107709	A	20040130	BG 2003-107709	20030408 <--
HK 1053644	A1	20060504	HK 2003-104217	20030612 <--
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US 7598268	B2	20091006		
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US 20050209456	A1	20050922	US 2005-92137	20050329
US 7335774	B2	20080226		

AU 2005202068	A1	20050602	AU 2005-202068		20050513
AU 2005202068	B2	20070809			
KR 2006036494	A	20060428	KR 2006-707122		20060413
KR 765841	B1	20071010	KR 2006-717401		20060828
JP 2007191486	A	20070802	JP 2007-62683		20070312
NO 2007001888	A	20030325	NO 2007-1888		20070412
IN 2008KN01705	A	20081226	IN 2008-KN1705		20080428
PRIORITY APPLN. INFO.:			US 2000-232159P	P	20000911
			AU 2001-293275	A3	20010911
			EP 2001-973722	A3	20010911
			EP 2005-17665	A3	20010911
			JP 2002-526851	A3	20010911
			US 2001-951265	A1	20010911
			WO 2001-US42131	W	20010911
			US 2002-284017	A1	20021030
			IN 2003-KN244	A3	20030226
			KR 2003-703558	A3	20030311
			US 2004-886950	A1	20040708

OTHER SOURCE(S): MARPAT 136:263158
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. of formulas I and II are provided [for I: Z = O, S, (un)substituted NH; Y = certain OH derivs., CHO, esters and amides of CO2H, certain NH2 derivs.; R1-R4 = H, halo, cyano, NO2, OH or derivs., NH2 or derivs., (un)substituted amidinyl, guanidinyl, alk(en/yn)yl, aryl, heterocyclyl, CHO, CO2H and esters and amides; R5-R8 = H, halo, NO2, OH or derivs., NH2 or derivs., SH or derivs., cyano, etc.; R9 = H, OH, (un)substituted alkoxy or aryloxy, NH2 or derivs., (un)substituted alkyl or aryl, CHO, alkanoyl, aroyl; for II: A, B, D, E = C or N, with at least one being N; Y = H, OH or derivs., SH or derivs., NH2 or derivs., cyano, various acyl groups, (un)substituted alk(en/yn)yl, aralkyl, heterocycloalkyl, aryl, etc.; R1-R8 = H, halo, NO2, cyano, OH or derivs., NH2 or derivs., acyl, SH or derivs., etc.; R9 = H, OH, (un)substituted alkoxy, aryloxy, NH2 or derivs., aryl, CHO, alkanoyl, aroyl]. Also provided are pharmaceutical formulations including the compds. or their pharmaceutically acceptable salts and a pharmaceutically acceptable carrier, which may be prepared by mixing the compds. or salts with a carrier and water. A disclosed method of treating a patient includes administering a pharmaceutical formulation according to the invention to a patient. Claims include tautomers of the compds., pharmaceutically acceptable salts, and pharmaceutically acceptable salts of the tautomers. I and II are inhibitors of receptor tyrosine kinases, and particularly of vascular endothelial growth factor receptor (VEGFR) tyrosine kinase. As such, they are inhibitors of angiogenesis, and thereby act as anticancer agents. Approx 270 invention compds. are listed, with detailed prepns. given for about 50 compds. Several general preparatory methods are discussed in detail. For instance, cyclocondensation of Et 2-(benzimidazol-2-yl)acetate with the corresponding ortho-amino nitrile (prepns. given), carried out in refluxing ClCH2CH2Cl in the presence of SnCl4, gave the invention quinolinone III. Many compds. I and II had in vitro IC50 values of less than 10 μM with respect to flt-1 (VEGFR1), KDR (VEGFR2) and bFGF kinases (recombinant, expressed in Sf9 insect cells).

OS.CITING REF COUNT: 10 THERE ARE 10 CAPLUS RECORDS THAT CITE THIS RECORD (10 CITINGS)
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L10        112 L9

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L12          5 L11 AND PD<20031107

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L12  ANSWER 1 OF 5  EMBASE  COPYRIGHT (c) 2009 Elsevier B.V. All rights
     reserved on STN
ACCESSION NUMBER:   2003481481  EMBASE
TITLE:              The impact of anti-angiogenic agents on cancer
                    therapy.
AUTHOR:             Marme, Dieter (correspondence)
CORPORATE SOURCE:   Tumor Biology Center, Institute of Molecular Oncology,
                    Breisacherstrasse 117, 79106 Freiburg, Germany. marme@tumor
                    bio.uni-freiburg.de
SOURCE:             Journal of Cancer Research and Clinical Oncology, (Nov
                    2003) Vol. 129, No. 11, pp. 607-620.
                    Refs: 89
                    ISSN: 0171-5216  CODEN: JCROD7
COUNTRY:            Germany
DOCUMENT TYPE:      Journal; General Review; (Review)
FILE SEGMENT:       016     Cancer
                    030     Clinical and Experimental Pharmacology
                    037     Drug Literature Index
                    038     Adverse Reactions Titles
LANGUAGE:           English
ENTRY DATE:         Entered STN: 29 Dec 2003
                    Last Updated on STN: 29 Dec 2003

L12  ANSWER 2 OF 5  EMBASE  COPYRIGHT (c) 2009 Elsevier B.V. All rights
     reserved on STN
ACCESSION NUMBER:   2003373828  EMBASE
TITLE:              Anti-cancer drug discovery and development
                    summit.
AUTHOR:             Blakey, David C. (correspondence)
```

CORPORATE SOURCE: AstraZeneca, Alderley Park, Macclesfield, Cheshire SK10 4TF, United Kingdom. david.blakey@astrazeneca.com
SOURCE: Expert Opinion on Investigational Drugs, (1 Sep 2003) Vol. 12, No. 9, pp. 1577-1582.
Refs: 15
ISSN: 1354-3784 CODEN: EOIDER
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article; (Conference paper)
FILE SEGMENT: 016 Cancer
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 2 Oct 2003
Last Updated on STN: 2 Oct 2003

AB The 5th Annual Anti-Cancer Drug Discovery and Development Summit brought together an international group of academic and industry scientists to discuss recent therapeutic developments in the field of oncology. The focus of the meeting was novel targeted approaches, i.e., those agents directed against targets that are overexpressed or overactive in tumour cells. It was acknowledged that cytotoxic agents will continue to play a key role in the treatment of cancer and new developments in this area were also discussed. With over 400 anticancer drugs in clinical development and a number of recent registrations, there is great optimism that significant therapeutic advances can be made.

L12 ANSWER 3 OF 5 EMBASE
ACCESSION NUMBER: 2003363876 EMBASE
TITLE: American Association for Cancer Research - 9th Annual Meeting: Investigating drugs: 11-14 July 2003, Washington, DC, USA.
AUTHOR: Mackay, Janie (correspondence); Williams, Laura
CORPORATE SOURCE: Thomson Current Drugs, Middlesex House, 34-42 Cleveland Street, London W1T 4JE, United Kingdom. laura.williams@current-drugs.com; janie.mackay@current-drugs.com
SOURCE: IDrugs, (1 Aug 2003) Vol. 6, No. 8, pp. 736-738.
ISSN: 1369-7056 CODEN: IDRUFN
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article; (Conference paper)
FILE SEGMENT: 016 Cancer
030 Clinical and Experimental Pharmacology
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
052 Toxicology
LANGUAGE: English
ENTRY DATE: Entered STN: 25 Sep 2003
Last Updated on STN: 25 Sep 2003

L12 ANSWER 4 OF 5 EMBASE
ACCESSION NUMBER: 2003276961 EMBASE
TITLE: Kinases - SMi Conference 9-10 April 2003, London, UK.
AUTHOR: Harrison, Ruth (correspondence)
CORPORATE SOURCE: Thomson Current Drugs, Middlesex House, 34-42 Cleveland Street, London W1T 4LB, United Kingdom. ruth.harrison@current-drugs.com
SOURCE: IDrugs, (1 Jun 2003) Vol. 6, No. 6, pp. 560-562.
ISSN: 1369-7056 CODEN: IDRUFN

COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article; (Conference paper)
FILE SEGMENT: 029 Clinical and Experimental Biochemistry
030 Clinical and Experimental Pharmacology
031 Arthritis and Rheumatism
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 24 Jul 2003
Last Updated on STN: 24 Jul 2003

AB Dr. Moss briefly summed up the conference by describing the growth in the development of kinase research over the years and the commitment being invested by companies aiming to find effective screening strategies. He closed the day by remarking on the new challenge for researchers of turning the concepts discussed into successful drugs.

L12 ANSWER 5 OF 5 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:501918 BIOSIS
DOCUMENT NUMBER: PREV200300498316
TITLE: Preclinical pharmacokinetics and metabolism of CHIR258, a potent tyrosine kinase inhibitor.
AUTHOR(S): Vora, Jayesh [Reprint Author]; Haroldsen, Peter [Reprint Author]; Renhowe, Paul [Reprint Author]; Heise, Carla [Reprint Author]; Steigerwalt, Ronald [Reprint Author]; Todd, Marque [Reprint Author]; Harris, Alex [Reprint Author]; Samara, Emil [Reprint Author]
CORPORATE SOURCE: Chiron Corporation, Emeryville, CA, USA
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (July 2003) Vol. 44, pp. 753. print.
Meeting Info.: 94th Annual Meeting of the American Association for Cancer Research. Washington, DC, USA. July 11-14, 2003.
ISSN: 0197-016X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 29 Oct 2003
Last Updated on STN: 29 Oct 2003

=> file registry

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	23.15	269.36

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-4.10

FILE 'REGISTRY' ENTERED AT 14:14:08 ON 30 NOV 2009

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 29 NOV 2009 HIGHEST RN 1194232-87-5
DICTIONARY FILE UPDATES: 29 NOV 2009 HIGHEST RN 1194232-87-5

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TSCA INFORMATION NOW CURRENT THROUGH June 26, 2009.

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  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=> s chir 258/cn
L13   1 CHIR 258/CN

=> d l13

L13 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2009 ACS on STN
RN   692737-80-7 REGISTRY
ED   Entered STN: 14 Jun 2004
CN   Propanoic acid, 2-hydroxy-, compd. with
     4-amino-5-fluoro-3-[6-(4-methyl-1-piperazinyl)-1H-benzimidazol-2-yl]-2(1H)-
     quinolinone (1:1) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   Propanoic acid, 2-hydroxy-, compd. with
     4-amino-5-fluoro-3-[5-(4-methyl-1-piperazinyl)-1H-benzimidazol-2-yl]-2(1H)-
     quinolinone (1:1) (9CI)
OTHER NAMES:
CN   CHIR 258
CN   Dovitinib lactate
CN   TKI 258
DR   1000873-96-0
MF   C21 H21 F N6 O . C3 H6 O3
SR   CA
LC   STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPATFULL

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     CRN 405169-16-6
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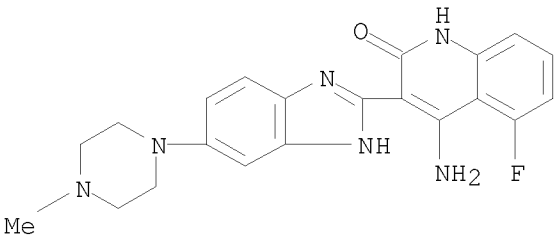

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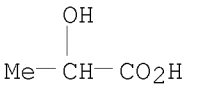

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

61 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
63 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	7.88	277.24

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-4.10

FILE 'CAPLUS' ENTERED AT 14:14:37 ON 30 NOV 2009

FILE COVERS 1907 - 30 Nov 2009 VOL 151 ISS 23
FILE LAST UPDATED: 29 Nov 2009 (20091129/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2009

CAplus now includes complete International Patent Classification (IPC) reclassification data for the third quarter of 2009.

CAS Information Use Policies apply and are available at:

http://www.cas.org/legal/infopolicy.html

This file contains CAS Registry Numbers for easy and accurate substance identification.

During November, try the new LSUS format of legal status information in the CA/CAplus family databases for free! Complete details on the number of free displays and other databases participating in this offer appear in NEWS 10.

=> s l13
L14 63 L13

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=> s l14 and (?cancer? or ?tumor? or ?tumour? or ?neoplasm?)
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        758861 ?TUMOR?
          6753 ?TUMOUR?
          6753 ?TUMOUR?
        759258 ?TUMOR?
                  (?TUMOR? OR ?TUMOUR?)
          6753 ?TUMOUR?
        758861 ?TUMOR?
        758861 ?TUMOR?
        759258 ?TUMOUR?
                  (?TUMOUR? OR ?TUMOR?)
        588351 ?NEOPLASM?
L15         48 L14 AND (?CANCER? OR ?TUMOR? OR ?TUMOUR? OR ?NEOPLASM?)

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       4773453 AD<20031107
                  (AD<20031107)
L16          2 L15 AND AD<20031107

=> d l16 1-2 ibib abs

L16  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:         2005:1242789  CAPLUS
DOCUMENT NUMBER:          143:477969
TITLE:                    Preparation of benzimidazole quinolinones for
                          inhibiting FGFR3 and treating multiple myeloma
INVENTOR(S):              Cai, Shaopei; Chou, Joyce; Harwood, Eric; Heise, Carla
                          C.; Machajewski, Timothy D.; Ryckman, David; Shang,
                          Xiao; Wiesmann, Marion; Zhu, Shuguang
PATENT ASSIGNEE(S):       Chiron Corporation, USA
SOURCE:                   U.S. Pat. Appl. Publ., 239 pp., Cont.-in-part of U.S.
                          Ser. No. 644,055.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   7
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
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     US 20050261307        A1    20051124    US 2004-983174          20041105
     US 20040092535        A1    20040513    US 2003-644055          20030819 <--
     US 7470709            B2    20081230
     CN 1692112            A     20051102    CN 2003-824565          20030819 <--
     US 20050203101        A1    20050915    US 2004-839793          20040505
     ZA 2006003598         A     20080430    ZA 2006-3598            20060505
     US 20090281100        A1    20091112    US 2008-317493          20081223
     US 20090181979        A1    20090716    US 2009-398130          20090304
PRIORITY APPLN. INFO.:                       US 2002-405729P     P   20020823
                                             US 2002-426107P     P   20021113
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                                             US 2003-644055      A2  20030819
                                             US 2003-517915P     P   20031107
                                             US 2003-526425P     P   20031202
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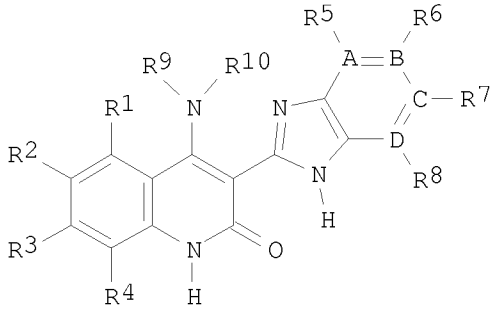
US 2003-526426P P 20031202
US 2004-546017P P 20040219
US 2004-982543 B1 20041105

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): MARPAT 143:477969

GI



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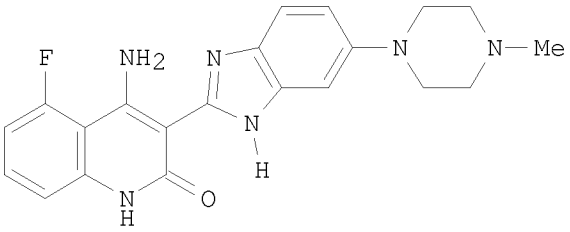

II

AB The title compds. I [A, B, C, and D = C, N; R1-R3 = H, halo, CN, NO2, etc.; R4 = H, alkyl; R5-R8 = H, halo, CN, NO2, etc.; R9 = H, (un)substituted alkyl, aryl, etc.; R10 = H], useful for inhibiting fibroblast growth factor receptor 3 or treating a biol. condition mediated by fibroblast growth factor receptor 3, were prepared E.g., a multi-step synthesis of 4-amino-5-fluoro-3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-quinolin-2-one (II), starting from 5-chloro-2-nitroaniline and 1-methylpiperazine, was given. The majority of the exemplary compds. I displayed an IC50 of less than 10 μM with respect to VEGFR1, VEGFR2, VEGFR3, FGFR1, CHK1, Cdc2, GSK-3, NEK-2, Cdk2, Cdk4, MEK1, NEK-2, CHK2, CK1ε, Raf, Fyn, Lck, Rsk2, PAR-1, c-Kit, c-ABL, p60src, FGFR3, FLT-3, PDGFRα, and PDGFRβ. In addition, many of the exemplary compds. exhibited IC50 values in the nM range and show potent activity with respect to VEGFR1, VEGFR2, VEGFR3, FGFR1, FGFR3, c-Kit, c-ABL, FLT-3, CHK1, Cdc2, GSK-3, NEK-2, Cdk2, MEK1, CHK2, Fyn, Lck, Rsk2, PAR-1, PDGFRα, and PDGFRβ with IC50 values of less than 1 μM. The mentioned above compound II was tested in various tests and showed significant antiproliferative activity. II inhibited FGFR3 receptor phosphorylation and ERK phosphorylation in multiple myeloma cell lines with activating FGFR3 mutations.

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

L16 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:1223876 CAPLUS

DOCUMENT NUMBER: 143:477966

TITLE: Preparation of benzimidazole quinolinones for inhibiting a checkpoint kinase 1 and their use in combination therapy for cancer

INVENTOR(S): Gesner, Thomas G.; Barsanti, Paul A.; Harrison, Stephen D.; Ni, Zhi-Jie; Brammeier, Nathan M.; Zhou, Yasheen; Le, Vincent P.
PATENT ASSIGNEE(S): Chiron Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 249 pp., Cont.-in-part of U.S. Ser. No. 644,055.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
US 20050256157	A1	20051117	US 2005-41191	20050121	
US 20040092535	A1	20040513	US 2003-644055	20030819	<--
US 7470709	B2	20081230			
CN 1692112	A	20051102	CN 2003-824565	20030819	<--
US 20050203101	A1	20050915	US 2004-839793	20040505	
US 20090281100	A1	20091112	US 2008-317493	20081223	

PRIORITY APPLN. INFO.:

US 2002-405729P	P	20020823
US 2002-426107P	P	20021113
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US 2002-428210P	P	20021121
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US 2003-478916P	P	20030616
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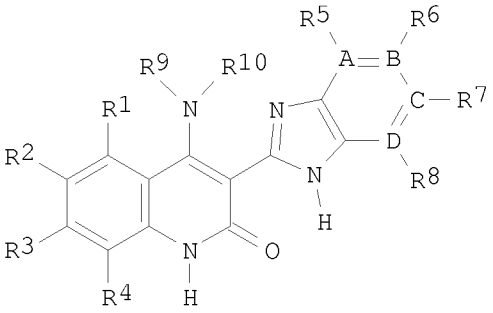
US 2004-538984P	P	20040123

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): CASREACT 143:477966; MARPAT 143:477966
GI



I

AB The title compds. [I; A, B, C, D = C, N; R1 = H, halo, CN, NO2, etc.; R2, R3 = H, halo, NO2, CN, etc.; R4 = H, (un)substituted alkyl; R5, R8 = H, (un)substituted alkyl, alkenyl, heterocyclyl; or R5 may be absent if A = N; or R8 may be absent if D = N; R6, R7 = H, halo, NO2, CN, etc.; R9 = H, (un)substituted alkyl, aryl, etc.; R10 = H; or R9 and R10 join together to form one or more rings, each having 5-7 members], useful for inhibiting checkpoint kinase 1, inducing cell cycle progression, and increasing apoptosis in cells, were prepared E.g., a multi-step synthesis of 4-amino-3-(benzimidazol-2-yl)-6-(4-methylpiperazinyl)hydroquinolin-2-one, was given. The compds. I were tested against various kinases. Two of the prepared compds. I, 4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-

benzimidazol-2-yl)-6-chloroquinolin-2-(1H)-one and 6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-4-[(piperidin-2-ylmethyl)amino]quinolin-2(1H)-one, were found to be potent inhibitors of CHK1 with IC50 of 0.32 nM and 0.63 nM, resp. The majority of the exemplary compds. I displayed an IC50 of less than 10 μM with respect to VEGFR1, VEGFR2, VEGFR3, FGFR1, CHK1, Cdc2, GSK-3, NEK-2, Cdk2, Cdk4, MEK1, NEK-2, CHK2, CK1ε, Raf, Fyn, Lck, Rsk2, PAR-1, c-Kit, c-ABL, p60src, FGFR3, FLT-3, PDGFRα, and PDGFRβ. In addition, many of the exemplary compds. exhibited IC50 values in the nM range and show potent activity with respect to VEGFR1, VEGFR2, VEGFR3, FGFR1, FGFR3, c-Kit, c-ABL, FLT-3, CHK1, Cdc2, GSK-3, NEK-2, Cdk2, MEK1, CHK2, Fyn, Lck, Rsk2, PAR-1, PDGFRα, and PDGFRβ with IC50 values of less than 1 μM. The compds. I may be used to prepare pharmaceutical compns. and may be used in conjunction with DNA damaging agents.

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

=> d his

(FILE 'HOME' ENTERED AT 13:58:33 ON 30 NOV 2009)

FILE 'REGISTRY' ENTERED AT 13:59:00 ON 30 NOV 2009
L1 STRUCTURE UPLOADED
L2 1 S L1
L3 34 S L1 FULL
L4 1 S L1 SSS

FILE 'CAPLUS' ENTERED AT 14:00:29 ON 30 NOV 2009
L5 70 S L3
L6 54 S L5 AND (?CANCER? OR ?TUMOR? OR ?TUMOUR? OR ?NEOPLASM?)
L7 5 S L6 AND AD<20031107

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L8 0 S L3

FILE 'REGISTRY' ENTERED AT 14:11:21 ON 30 NOV 2009
SET SMARTSELECT ON
L9 SEL L3 1- CHEM : 42 TERMS
SET SMARTSELECT OFF

FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 14:11:23 ON 30 NOV 2009
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L11 97 S L10 AND (?CANCER? OR ?TUMOR? OR ?TUMOUR? OR ?NEOPLASM?)
L12 5 S L11 AND PD<20031107

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L13 1 S CHIR 258/CN

FILE 'CAPLUS' ENTERED AT 14:14:37 ON 30 NOV 2009
L14 63 S L13
L15 48 S L14 AND (?CANCER? OR ?TUMOR? OR ?TUMOUR? OR ?NEOPLASM?)
L16 2 S L15 AND AD<20031107

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Executing the logoff script...

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	17.70	294.94

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-1.64	-5.74

STN INTERNATIONAL LOGOFF AT 14:15:30 ON 30 NOV 2009